REMARKS

The invention provides, *inter alia,* bicyclic heterocycles, processes for their preparation and their use as herbicides and pharmaceutical agents. It had been unexpectedly discovered that these bicyclic heterocycles exhibit AMPDA and ADA inhibition activity, especially in plants. Applicants believe that the invention discloses valuable tools, such as functional assays, which may be used by one skilled in the art for measuring the efficacies of the instant inhibitors in *vivo* but also where the inhibitors are applied in vitro to AMPDA and ADA enzymes are extracted from plants or otherwise produced.

Pursuant to the provisions of 37 C.F.R. §§ 1.17(a) and 1.136(a), Applicants petition the Assistant Commissioner to extend the time period for Applicants to respond to the outstanding Office Action by three (3) months, i.e., up to and including July 12, 2005. A check for $1020.00 is enclosed with this paper. Applicants authorize the Director to charge any additional fee for consideration of this paper, or credit any overpayment, to Deposit Account No. 50-0320.

Applicants thank the Examiner for removing the rejections of claims 7 and 18-20 under 35 U.S.C.§ 102 (b) over Duffy et al., and for indicating that claims 1-3 and 5-17 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. §112.

Claims 1-3 and 5-17 are pending in this application. In order to advance prosecution, claims 1, 3, 5, 7, 8, 9 and 11 are amended without prejudice to Applicant's position as to the patentability of the claimed subject matter as originally presented. Applicants respectfully point out that in addition to correcting various formal matters, amendments to claim 1 specify that instant method is now directed to the inhibition of AMPDA and ADA enzymatic activity in plants. Further, claims 7, 9 and 11 are rewritten to include the definitions of formula (I,) and

claims 3, 5 and 8 are amended to correct formal matters. These amendments are supported throughout the specification and therefore, no new matter is present.

Claims 1-3 and 5-17 are rejected under 35 U.S.C. §112, first paragraph, for allegedly not being enabled. In view of the amendments to claims 1 and remarks submitted below, Applicants request the reconsideration and withdrawal of the rejections.

As to claim 1, the Office Action contends that "claim 1 is apparently directed to a method of treating and therefore is incomplete for failure to specify either a specific disease condition being treated by said administration or --a host in need thereof" (Office Action page 5). Applicants respectfully point out that in order to advance prosecution and to achieve a reasonable compromise with the Examiner, amendments to claim 1 specify that enzymatic inhibition of AMPDA and ADA occurs in a specific host in need thereof, such as plants. This feature of the invention is clearly demonstrated by the biological examples; see Chapter C (Biol. Examples), sect. 1, subsect. A, and Chapter C, sect. 2 and 3. Applicants make these amendments without prejudice to their right to file a divisional application to the cancelled subject matter.

Moreover, contrary to the Examiner's allegations, Applicants urge that although formula (I) encompasses a large number of individual compounds the structure of the compounds is rather similar from the structural elements combined. The compounds have a core structure which is common to all compounds of formula (I), namely the bicyclic heterocyclic system linked to a hydrocarbon bridge which in turn is substituted by very polar functional groups.

The examples show a similar effect of the compounds even if the group G-L is varied widely (see different definitions of A and G-L in the compounds 1-1, 12-1, 21-1, 21-3, 22-2, 28-1, 44-1 and 159-3). Furthermore, the tables provide even more structurally similar examples and thus provide guidance for the person skilled in the art to make other compounds similar to

those having already shown a specific enzyme inhibiting effect. Applicants urge that in view of the variation of structural elements in the existing biological examples and in view of the structural similarities of these examples, a skilled artisan would have sufficient reasons to believe that other variation within the claimed group of compounds would result in the inhibiting effects too and would not require additional experimentation to deduce the function of these compounds.

Additionally, the group of heterocyclic rings involved in the basic core of formula (I) is rather limited and some of the heterocyclic systems are even tautomers or stereoisomers of other heterocyclic systems.

Furthermore, it should be emphasized that the inhibition of AMPDA and ADA enzymes in plants by instant compounds of formula (I) has never been shown previously, but is clearly demonstrated by biological examples of the instant application. Applicants urge that in addition to providing a group of compounds with the demonstrated inhibitory effect, the instant invention provides the assays which can be used for detecting specific inhibitors as described in details in Chapter C section 1 of the instant application. Accordingly, Applicants urge that since the novel inhibitory effect is clearly described in the instant specification and examples, one skilled in the art would be able to easily adapt the instant application method and optimize the effects without additional experimentation in order to practice the instant invention

Thus, and contrary to the allegations in the Office Action, undue experimentation would not be necessary to practice the instantly claimed invention. Consequently, reconsideration and withdrawal of the Section 112, first paragraph, rejection for alleged lack of enablement are respectfully requested.

Claims 1-3 and 5-17 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. In view of the amendments to claims 1,3,5,8, 9 and 11, and remarks submitted below, Applicants request the reconsideration and withdrawal of the rejections.

As to **claim 1,** lines 54-55, in order to advance prosecution, Applicants amended claim 1 to exclude N from the definition of a heteroatom. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

As to **claim 1** lines 73-74, in order to advance prosecution, in addition to amendments made in the previous response, Applicants now amend claim 1 to further clarify that the term "heterocyclyl" is a radical derived from a heterocyclic ring. Accordingly, Applicants request reconsideration and withdrawal of the rejections.

As to **claim 8** line 8, the Office Action asserts that in view of the decision on Regents of the University of California v. Eli Lilly (119F.3d 1559 at 1568; 43 USPQ2d 1398 at 1406 (Fed. Cir 1997)), the variable "Z" is not completely described in the claim. Applicants respectfully disagree.

Applicants urge that the present definition of variable Z is not "a definition by function alone". In fact, the instant process is defined by structure of the final product, particular position at the molecule where the last modification takes place, and by the the functional group to be prepared at said position.

Applicants further urge that the definition is clear as the functional term "Z" is a precursor of the radical G-L" and is further illustrated in the description e. g. at page 30, lines 1 to 26. The possible reactions are derivatization reactions customary to persons skilled in the art and determined by the synthethic goal G-L.

Particularly, emphasis is given there e.g. to customary protection groups for hydroxyl or amino groups. Thus, Applicants believe that one skilled in the art would know enough synthetic ways to follow this general pattern. An important step lies in the method wherein the reduction of the bicyclic system is effected on a compound having a group Z instead of the different group G-L at the respective position rather than in the particular reaction from the precursor to the group G-L. Moreover, the radical Z is defined by the final group G-L to which it has to be transformed. Applicants, thus, do not believe that it is necessary to define the structure of Z explicitly because it is indirectly defined by structural limitations of the final product. This, however, is not the case in Regents of the University of California v. Eli Lilly where only the biological function was used to define the product.

As to **claims 8, 9 and 11**, Applicants believe that the terms objected to are defined sufficiently in the description. With respect to the term "modifying" and the like mentioned, such as "cyclizing", and "condensing", it has to be noted that the specific modification steps are known to a person skilled in the art of chemistry and are not a specific contribution according to the invention which, however, is mainly in the structure of the final product as an active ingredient. The process steps are defined by the structure of the reacting moieties of the starting materials, the structures of the reaction products, and by the type of reactions. It is urged that the person skilled in the art realizes easily which bonds are formed and broken during the cyclization, modification and reduction. The description provides sufficient hints how to make the compounds (see pages 28-38 of the description)

It is further urged that specifying the process claims with respect to the functional terms would limit the scope of the process arbitrary. As far as the process of claim 8 is concerned the

invention is in the preparation of novel final products of claim 7. Therefore, the process can be an analogous process and should be considered patentable.

It is also urged that the definition of G-L is not incomplete as alleged by the Examiner. Therefore, the process claims are also not incomplete. The processes of claims 9 and 11 are additionally based on separate inventive merit (independent from the final novel products of claim 7), as discussed previously and in the description. Accordingly, Applicants request reconsideration and withdrawal of these rejections.

As to claim 5, in order to advance prosecution, the claim is amended to specify the number of carbon atoms in the hydrocarbon bridge. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

Claims 7, 8, 9, 11 and 13-17 are now rejected under 35 U.S.C. 112, fourth paragraph, as allegedly being of improper dependent form. Applicants urge that in order to advance prosecution and to achieve a reasonable compromise with the Examiner, the claims 7, 9 and 11 are rewritten to include the limitations of formula I as described in claim 1.

The Office Action states further that the Applicant may address the rejection of claims 13-17 by specifying plants as hosts. Applicants urge that amendments to claim 1, which specify that enzymatic inhibition of AMPDA and ADA occurs in plants, render the rejection moot.

As to formal objections to claim 1, as set forth at page 8 of the Office Action, Applicant respectfully disagree with these criticisms, and respectfully remind the Examiner that the definition in lines 8 and 9 of claim 1 reads:

" E a) in the case that D is a nitrogen atom, is a nitrogen atom or a group of the formula C-R°, where R° is as defined further below, or "

Accordingly, E is a nitrogen atom or C-R°, whenever D is a nitrogen atom. The double occurrence of "is a nitrogen atom" is thus necessary, because otherwise the definition of E would be missing for the case where D is a nitrogen atom. Accordingly, Applicants believe that the objection to claim 1 is improper and should be removed.

As to the formal objections to claim 7, Applicants urge that in the claim 7, the disclaimer defines a compound of formula (I) in which A = CH, D = C, E = NH and G - L is ß-D-ribofuranosyl. Since D = C, the disclaimed compound is thus within the definition of formula (I) of claim 1, where E has to be selected from alternative b) (in case D is a carbon atom). According to alternative b), E is a group of the formula N-R°, O, S, SO or SO_2. Further, since R° can be hydrogen, E can be "NH". Thus, Applicants urge that claim 7 has proper antedecent basis in claim 1.

As to the formal objections to claim 8, Applicants urge that in claim, lines 1 and 2, reference is made to compound of formula (I) as claimed in claim 7. This ensures that the process of claim 8 is defined as a process for the preparation of specific novel compounds of formula (I) as described in claim 7, and not of all compounds of formula (I) as defined in claim 1. Thus, Applicants respectfully point out that the reference to formula (I) in the last line of claim 8, refers to formula (I) as defined in claim 7. However, in order to advance prosecution and further clarify matters, Applicants amend claim 8 by changing "formula (I)" (see last line of claim 8) to "said compound of formula(I)". Applicants further urge that the definition of the compounds of formulae (II), (III), (III'), (III"), (III"') depends not only on the definition of formula (I) but must be consistent with the specific compound of formula (I) to be prepared, for example compound of formula (I) as defined in claim 7.

As to the formall objections to claim 3, Applicant urge that in order to advance prosecution and to further clarify formal matters, Applicants have amended claim 3 to specify that definition of variables R1 and L* are according to those described in claim 1.

Accordingly, Applicants request reconsideration and withdrawal of these objections.

Accordingly, in view of the foregoing, reconsideration of all rejections in this application is requested and favorable action is solicited.

Respectfully submitted,

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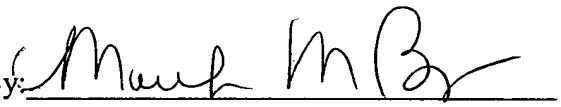
By: 

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